PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

2619

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/003175	24.03.2005	26.03.2004

International Patent Classification (IPC) or both national classification and IPC
A61K9/26, A61K9/58, A61K31/403

Applicant
LEK PHARMACEUTICALS D.D.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 33-36

because:

☒ the said international application, or the said claims Nos. 33-36 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/003175

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-36
	No:	Claims	1
Inventive step (IS)	Yes:	Claims	2-36
	No:	Claims	1
Industrial applicability (IA)	Yes:	Claims	1-32
	No:	Claims	

2. Citations and explanations

see separate sheet

Reference is made to the following document:

D1: MORIGUCHI M ET AL: "THERAPEUTIC EFFECTS OF LK 423, A PHTHALIMIDO-DESMURAMYL-DIPEPTIDE COMPOUND, ON DEXTRAN SULFATE SODIUM INDUCED COLITIS IN RODENTS THROUGH RESTORING THEIR INTERLEUKIN-10 PRODUCING CAPACITY" ARZNEIMITTEL FORSCHUNG. DRUG RESEARCH, EDITIO CANTOR VERLAG, AULENDORF, DE, vol. 49, no. 1, 1999, pages 184-192

Item III

Claims 33-36 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Item V

1 Novelty

The subject matter of claim 1 is not regarded as new in the sense of Article 33(2) PCT.

D1 already discloses a subcutaneous injectable dosage form comprising N-(2-(2-phthalimidoethoxy) acetyl)-L-alanyl-D-glutamic acid (= LK-423) (see page 185, column 2, paragraph 2).

2 Inventive Step

The subject-matter of claims 2-36 seems to be new in the sense of Article 33(2) PCT and involves an inventive step in the sense of Article 33(3) PCT in view of the present prior art.

The problem to be solved in the present application is the provision of gastro-resistant pharmaceutical dosage forms comprising N-(2-(2-phthalimidoethoxy) acetyl)-L-alanyl-D-glutamic acid (= LK-423).
The solution provided are gastroresistant-coated dosage forms like microcapsules or tablets.

Closest prior is D1 describing a subcutaneous injectable formulation of LK-423 (see page 185, column 2, paragraph 2). There is no hint given that LK-423 may be formulated in gastroresistant-coated dosage forms like microcapsules or tablets.

Hence, the subject-matter of present claims 2-36 is new and inventive.

3 Industrial applicability

For the assessment of the present claims 33-36 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The subject matter of claims 1-32 is industrially applicable in the sense of Article 33(4) PCT.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/003175

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

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3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 33-36

because:

☒ the said international application, or the said claims Nos. 33-36 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
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the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/003175

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-36
	No:	Claims	1
Inventive step (IS)	Yes:	Claims	2-36
	No:	Claims	1
Industrial applicability (IA)	Yes:	Claims	1-32
	No:	Claims	

2. Citations and explanations

see separate sheet

Reference is made to the following document:

D1: MORIGUCHI M ET AL: "THERAPEUTIC EFFECTS OF LK 423, A PHTHALIMIDO-DESMURAMYL-DIPEPTIDE COMPOUND, ON DEXTRAN SULFATE SODIUM INDUCED COLITIS IN RODENTS THROUGH RESTORING THEIR INTERLEUKIN-10 PRODUCING CAPACITY" ARZNEIMITTEL FORSCHUNG. DRUG RESEARCH, EDITIO CANTOR VERLAG, AULENDORF, DE, vol. 49, no. 1, 1999, pages 184-192

Item III

Claims 33-36 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Item V

1 Novelty

The subject matter of claim 1 is not regarded as new in the sense of Article 33(2) PCT.

D1 already discloses a subcutaneous injectable dosage form comprising N-(2-(2-phthalimidoethoxy) acetyl)-L-alanyl-D-glutamic acid (= LK-423) (see page 185, column 2, paragraph 2).

2 Inventive Step

The subject-matter of claims 2-36 seems to be new in the sense of Article 33(2) PCT and involves an inventive step in the sense of Article 33(3) PCT in view of the present prior art.

The problem to be solved in the present application is the provision of gastro-resistant pharmaceutical dosage forms comprising N-(2-(2-phthalimidoethoxy) acetyl)-L-alanyl-D-glutamic acid (= LK-423).
The solution provided are gastroresistant-coated dosage forms like microcapsules or tablets.

Closest prior is D1 describing a subcutaneous injectable formulation of LK-423 (see page 185, column 2, paragraph 2). There is no hint given that LK-423 may be formulated in gastroresistant-coated dosage forms like microcapsules or tablets.

Hence, the subject-matter of present claims 2-36 is new and inventive.

3 Industrial applicability

For the assessment of the present claims 33-36 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

The subject matter of claims 1-32 is industrially applicable in the sense of Article 33(4) PCT.